

An Unusual Case of Shock in a 5 Week Old Male

AUGUST 26, 2020

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A case of unexplained shock in a 32 day old male

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8/24/2020

Case Presentation

- **A 32 day old male presented to an Emergency Department (ED) after becoming limp and unresponsive.**
- **He was hypotensive, hypothermic, bradycardic, oliguric, hypoxic, and hypoglycemic.**
- **He was resuscitated with Normal Saline boluses (60 cc/kg), 10% dextrose infusion, and positive pressure ventilation.**
- **He was evaluated for serious bacterial and viral infection and empirically administered broad spectrum antibiotics.**
- **He was transferred to a Pediatric Intensive Care Unit (PICU) at a tertiary referral center.**

Birth History

- **He was delivered vaginally at 39 weeks gestation.**
- **The delivery was complicated by meconium aspiration and a nuchal cord.**
- **He spent a few hours on CPAP in the Neonatal Intensive Care Unit (NICU) but was discharged from the Well Baby Nursery.**
- **His birthweight was 2590 grams, which was deemed to be appropriately sized for gestational age.**
- **The NICU course was complicated by hypoglycemia which responded to oral glucose administration.**

Past Medical History

- After 7 days of life, he developed unusual desquamation on his hands and feet in a stocking glove pattern along with some other generalized desquamation.
- He would occasionally bleed from his nose and lips.
- His mother noticed prolonged bleeding from his circumcision.
- He did not feed very well.
- He never regained his birth weight.
- His normal newborn screen was unremarkable.

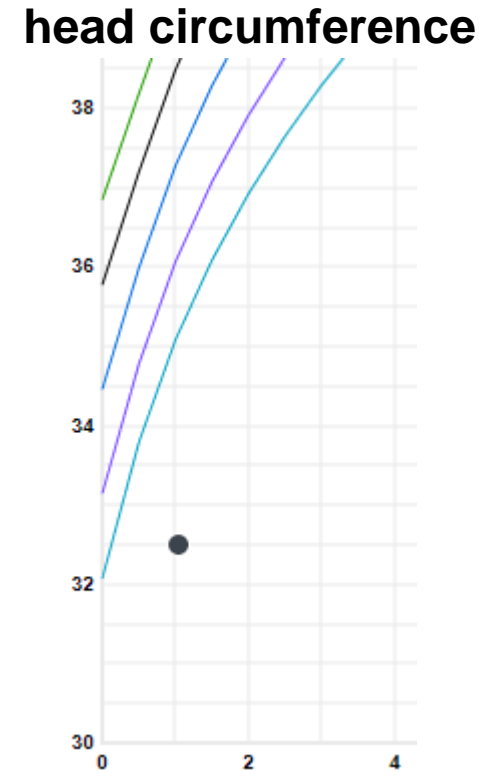
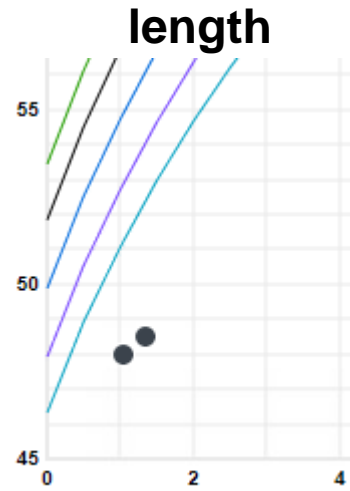
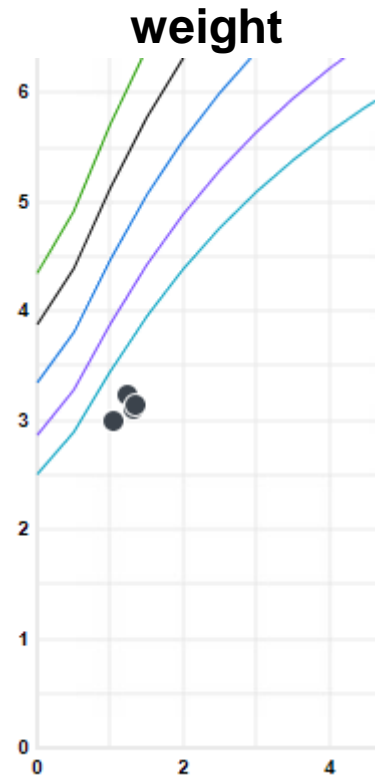
Family/Social History

- **Initially these seemed to be noncontributory.**
- **The patient's mother and the referring ED reported prenatal screens for sexually transmitted infections (STI) were negative.**

Examination in PICU

- **Intubated**
- **Very small**
- **Ugly raw desquamation on hands and feet**
- **Prominent liver**
- **Desquamative, bleeding lesion on anus**
- **Bleeding lips**
- **Anasarca**
- **Prolonged oozing from phlebotomy and IV sites.**

Growth Parameters



Hands and Feet



Initial Laboratory Findings

- Hypoglycemia
- Hyponatremia
- Hyperkalemia
- Inappropriately low cortisol
- Anemia
- Thrombocytopenia
- Hypofibrinogenemia
- Elevated PT and PTT
- Hypoalbuminemia
- Isolated AST elevation
- CRP elevation

Initial Diagnostic Impressions

- **Working diagnosis: Sepsis with shock and respiratory failure**
 - **Serious bacterial infection: Bacteremia, UTI, Meningitis, Pneumonia**
 - **Serious viral infection: Neonatal Herpes Simplex Virus (HSV) Disease**
 - **Toxin mediated syndrome: TSS, SSSS**
- **Differential diagnosis:**
 - **Metabolic crisis complicating an inborn error of metabolism**
- **Underlying diagnoses considered:**
 - **Epidermolysis bullosa**
 - **Bleeding disorder**

Initial PICU Management

- **Broad spectrum antibiotic and antiviral therapy**
 - Urine, Blood, Cerebrospinal Fluid (CSF) cultures were sterile.
 - HSV nucleic acids were not detected in CSF or cutaneous lesions.
 - The patient remained intermittently hypothermic.
- **Blood product transfusions**
 - Consumption of platelets and fibrinogen persisted.
- **10% dextrose infusion and hydrocortisone administration**
 - Even brief interruptions in infusion resulted in hypoglycemia.
- **Mechanical ventilation**
 - PICU successfully extubated the patient, but he remained hypoxic.
- **Wound cares for hands and feet**
 - Desquamation persisted.

Consulting Service Contributions

- **Pediatric Endocrinology:**
 - Demonstrated thyroid hormone, insulin-like-growth-factor-1, and testosterone were also inappropriately low.
- **Pediatric Hematology/Oncology:**
 - Excluded a bleeding disorder.
- **Pediatric Infectious Diseases:**
 - Recommended an evaluation for congenital infection.

Diagnosis

Syphilis IgM and IgG screen was positive

RPR titer was > 1:256

Hospital Course

- **Syphilis was treated with 10 days of IV Penicillin G at 300,000 Units/kg/day.**
- **Screening for HIV was ordered and was negative.**
- **Hypothyroidism was treated with Levothyroxine.**
- **Adrenal insufficiency was treated with hydrocortisone.**
- **Growth Hormone deficiency was treated with Growth Hormone.**

Short Term Outcomes

- Coagulopathy, anemia, and thrombocytopenia resolved.
- Hypoglycemia resolved and electrolytes normalized.
- Hypoxia and temperature instability resolved.
- CSF VDRL proved to be reactive, proving neurosyphilis.
- An MRI of the Brain demonstrated ischemic insults.
- Long bone films demonstrated periostitis and osteochondritis.
- The patient's eye examination was normal, but he failed a hearing screen.

Long Bone Films



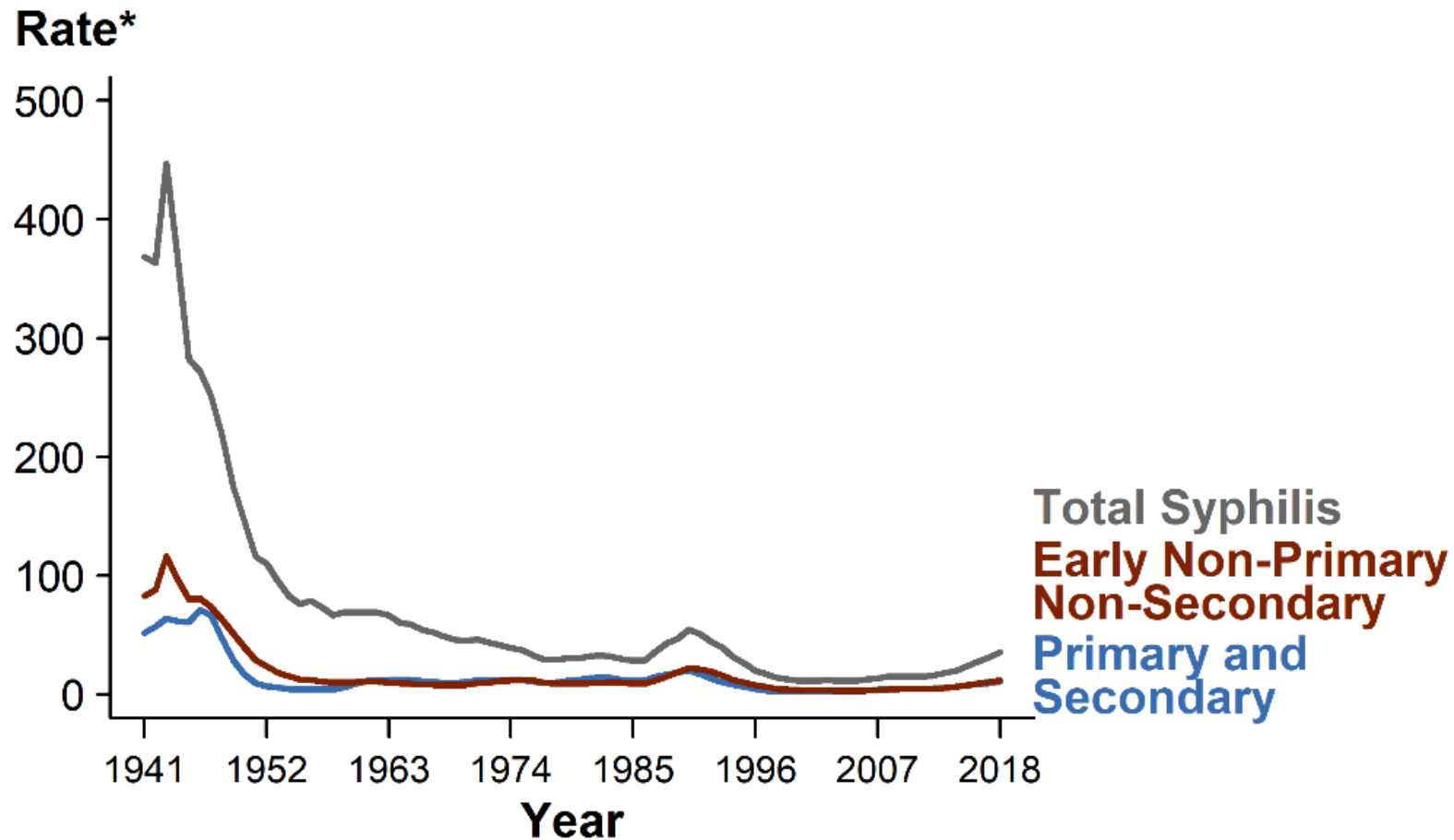
Pathogenesis

- **Intrauterine or congenital infection with syphilis, leading to neurosyphilis and multisystem organ disease,**
- **Leading to hypophysitis,**
- **Leading to pituitary failure,**
- **Leading to hypoglycemia and metabolic crisis and synthetic liver dysfunction and coagulopathy and growth failure,**
- **Leading to shock,**
- **Leading to CNS ischemia**

Long Term Follow Up

- The RPR will be trended every 2 to 3 months.
- If the RPR is stable or rising after 6 to 12 months, the infant will be retreated.
- A CSF examination will be performed 6 months from completion of therapy.
- If CSF parameters are abnormal, the infant will be retreated.
- If the CSF VDRL is reactive, the infant will be retreated.
- An MRI Brain will be repeated at that time for prognostication.
- Serial ophthalmology examinations will be required to look for optic atrophy.
- A formal ABR will be required to prove or disprove sensorineural hearing loss.
- Early Intervention enrollment will be recommended.

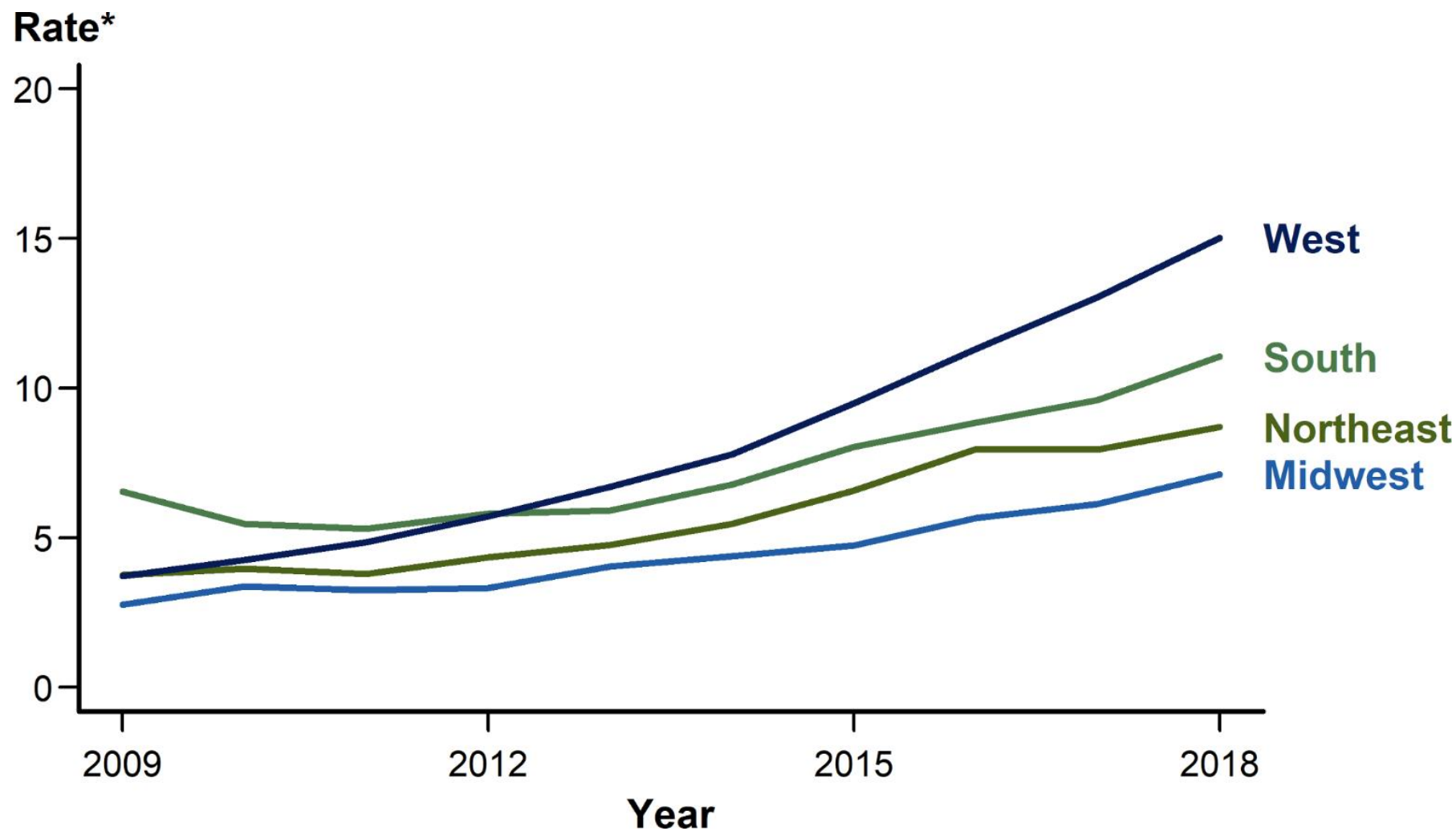
Figure 35. Syphilis — Rates of Reported Cases by Stage of Infection, United States, 1941–2018



* Per 100,000.

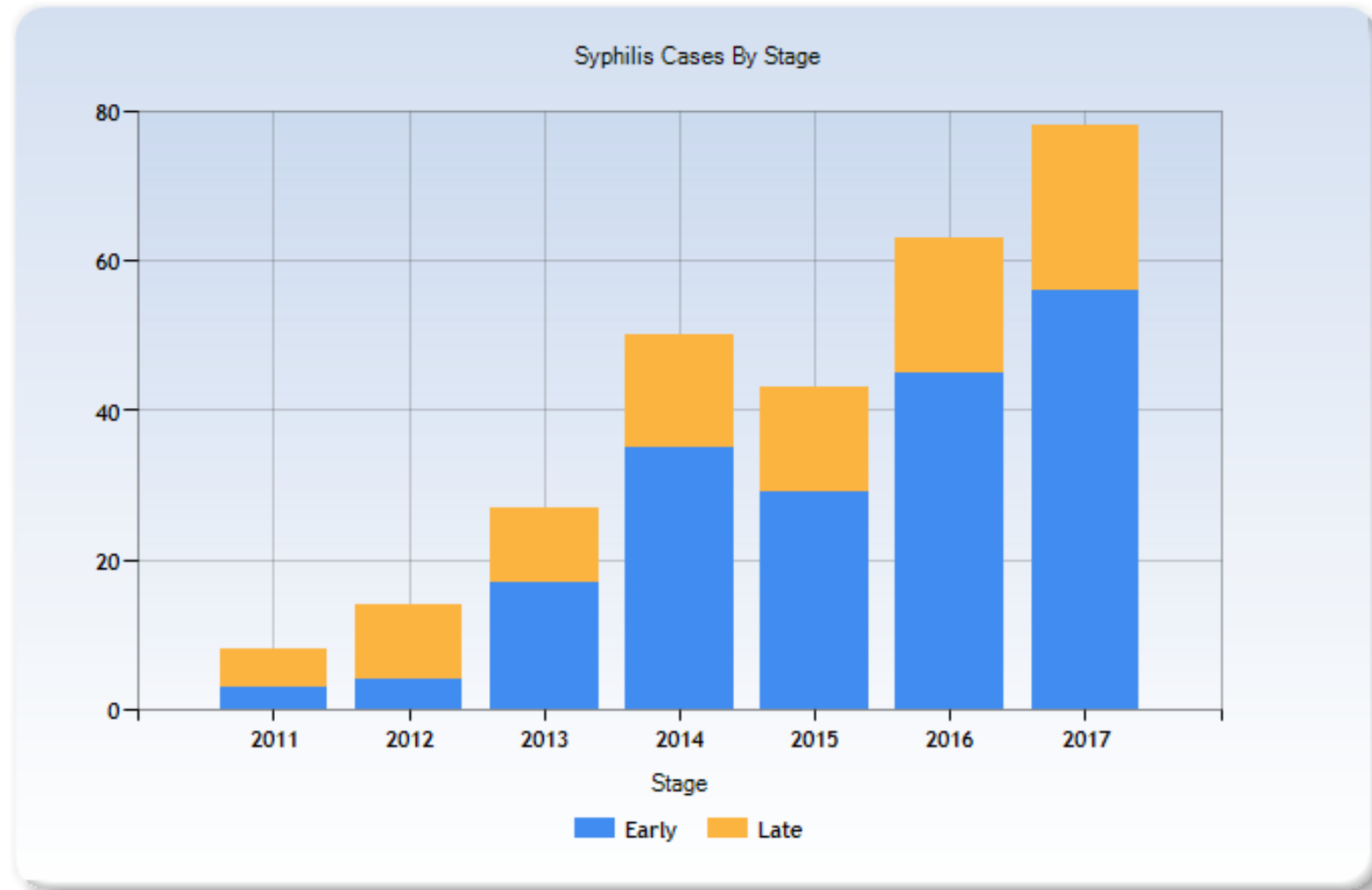
NOTE: See section A1.3 in the Appendix for more information on syphilis case reporting.

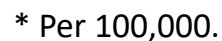
Primary and Secondary Syphilis — Rates of Reported Cases by Region, United States, 2009–2018



* Per 100,000.

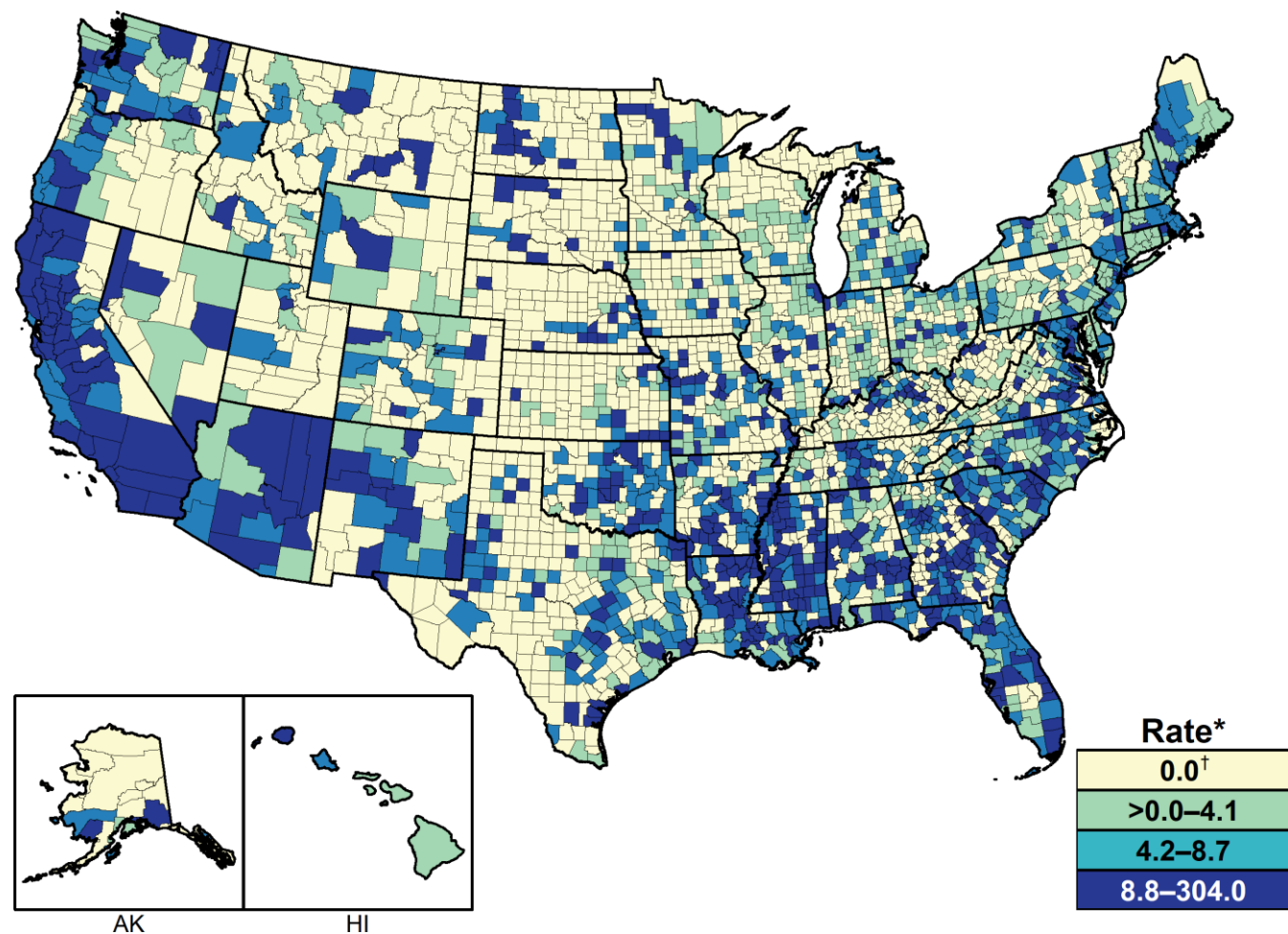
North Dakota Syphilis Cases





NOTE: Section A1.11 in the Appendix for more information on interpreting reported rates in US territories.

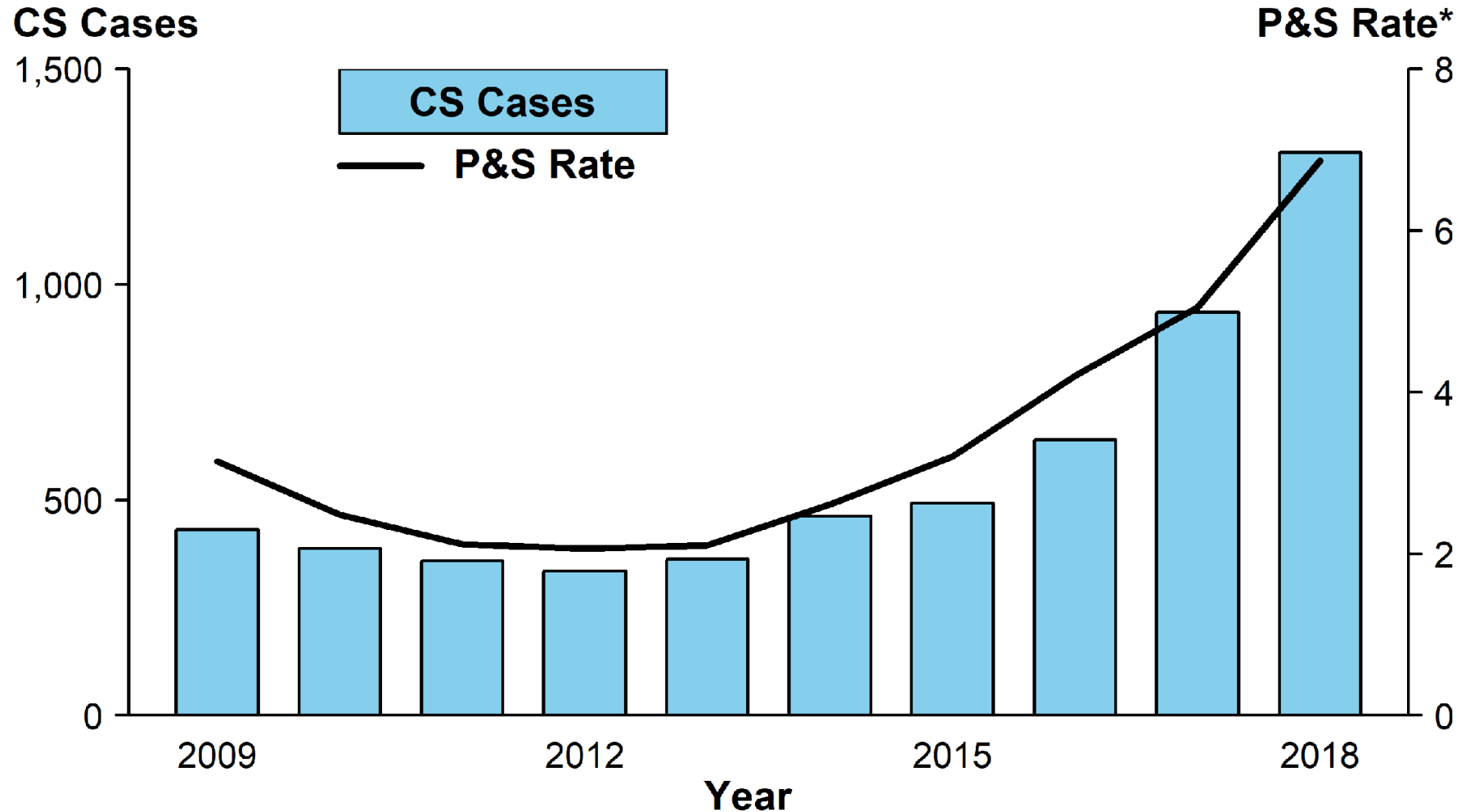
Primary and Secondary Syphilis — Rates of Reported Cases by County, United States, 2018



* Per 100,000.

[†] In 2018, 1,498 (47.7%) of 3,142 counties in the United States reported no cases of primary and secondary syphilis. See section A1.4 in the Appendix for more information on county-level rates.

Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Females Aged 15–44 Years, United States, 2009–2018



* Per 100,000.

ACRONYMS: CS = Congenital syphilis; P&S = Primary and secondary syphilis.



A Quick Review of Acquired Syphilis

Syphilis Stages



Example of a primary syphilis sore



Secondary rash from syphilis on palms of hands



Secondary rash from syphilis on torso

1. **Primary: Painless ulcer**
2. **Secondary: Funny rash**
3. **Early latent: No symptoms < 1 year from infection**
4. **Late latent: No symptoms > 1 year from infection**
5. **Tertiary (gummatous disease)**
6. **Unknown duration**

Neurosyphilis can occur at any stage of syphilis

Stigmata of Congenital Syphilis

- **Hepatosplenomegaly**
- **Snuffles (nasal discharge)**
- **Lymphadenopathy**
- **Mucocutaneous lesions**
- **Rash**
- **Pneumonia**
- **Growth restriction**
- **Stillbirth**
- **Edema**
- **Hemolytic anemia**
- **Thrombocytopenia**
- **Osteochondritis**
- **Periostitis**
- **Pseudo-paralysis**
- **Funisitis**
- **Chorioamnionitis**

Most likely presentation of Congenital Syphilis

Asymptomatic healthy looking baby.

Late Sequelae of Congenital Syphilis

- **8th cranial nerve deafness**
- **Blindness (interstitial keratitis, uveitis, optic atrophy)**
- **Neurocognitive and neuromuscular disability.**
- **Dental**
 - **Peg shaped notched central incisor (Hutchinson teeth)**
 - **Mulberry molars**
- **Perioral fissures (rhagades)**
- **Skeletal**
 - **Frontal bossing**
 - **Saddle nose**
 - **Symmetric painless swelling of the knees (Clutton's Joints)**

Missed Opportunities for Prevention of Congenital Syphilis — United States, 2018

Anne Kimball, MD^{1,2}; Elizabeth Torrone, PhD²; Kathryn Miele, MD^{2,3}; Laura Bachmann, MD²; Phoebe Thorpe, MD²; Hillard Weinstock, MD²; Virginia Bowen, PhD²

TABLE 1. Demographic and clinical characteristics of infants with congenital syphilis and their mothers, by U.S. Census region* — United States, 2018

Characteristic	Census region No. (% [†])				
	Total	South	West	Midwest	Northeast
Race/Ethnicity of mother[§]					
White	286 (21.9)	117 (17.1)	130 (28.0)	29 (28.2)	10 (18.9)
Black	510 (39.1)	346 (50.5)	86 (18.5)	54 (52.4)	24 (45.3)
Hispanic	411 (31.5)	200 (29.2)	194 (41.7)	6 (5.8)	11 (20.7)
American Indian/Alaska Native	29 (2.2)	2 (0.3)	23 (4.9)	4 (3.9)	0 (0)
Asian/Pacific Islander	26 (2.0)	3 (0.4)	17 (3.7)	5 (4.9)	1 (1.9)
Other/Unknown	44 (3.4)	17 (2.5)	15 (3.2)	5 (4.9)	7 (13.2)
Maternal stage of syphilis					
Primary or secondary	108 (8.3)	48 (7.0)	43 (9.2)	11 (10.7)	6 (11.3)
Early non-primary non-secondary	400 (30.6)	203 (29.6)	128 (27.5)	45 (43.7)	24 (45.3)
Unknown duration or late	664 (50.8)	317 (46.3)	283 (60.9)	43 (41.7)	21 (39.6)
Other/Missing	134 (10.3)	117 (17.1)	11 (2.4)	4 (3.9)	2 (3.8)
Infant outcomes					
Live-born with signs or symptoms of congenital syphilis [¶]	434 (33.2)	167 (24.4)	198 (42.6)	46 (44.7)	23 (43.4)
Live-born with no documented signs or symptoms of congenital syphilis	788 (60.3)	474 (69.2)	236 (50.8)	52 (50.5)	26 (49.1)
Stillborn	78 (6.0)	41 (6.0)	29 (6.2)	4 (3.9)	4 (7.5)
Unknown vital status	6 (0.5)	3 (0.4)	2 (0.4)	1 (1.0)	0 (0)
Total	1,306	685	465	103	53

* South: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia; West: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming; Midwest: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin; Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont.

[†] Percentages might not sum to 100 because of rounding.

[§] Whites, blacks, American Indians/Alaska Natives, Asians/Pacific Islanders, and others/unknown were non-Hispanic; Hispanics could be of any race.

[¶] Signs or symptoms of congenital syphilis include any one of the following: condyloma lata, snuffles, syphilitic rash, hepatosplenomegaly, jaundice/hepatitis, pseudoparalysis, or edema on physical exam; long-bone radiograph findings consistent with congenital syphilis; abnormal protein or white blood cell count in the cerebrospinal fluid; reactive venereal disease research laboratory test in the cerebrospinal fluid; direct detection of *Treponema pallidum* by dark field microscopy or special stains.

Treatment of Pregnant Woman

Primary, Secondary, and Early Latent Syphilis:

1 dose of 2.4 million Units of Intramuscular Benzathine Penicillin G

Late Latent Syphilis, Tertiary Syphilis, or Syphilis of Unknown Duration:

3 doses of 2.4 million units of Intramuscular Benzathine Penicillin G

Each dose must be 7 days apart.

The doses cannot be less than 7 days apart and cannot be more than 7 days apart.

From: **Syphilis**

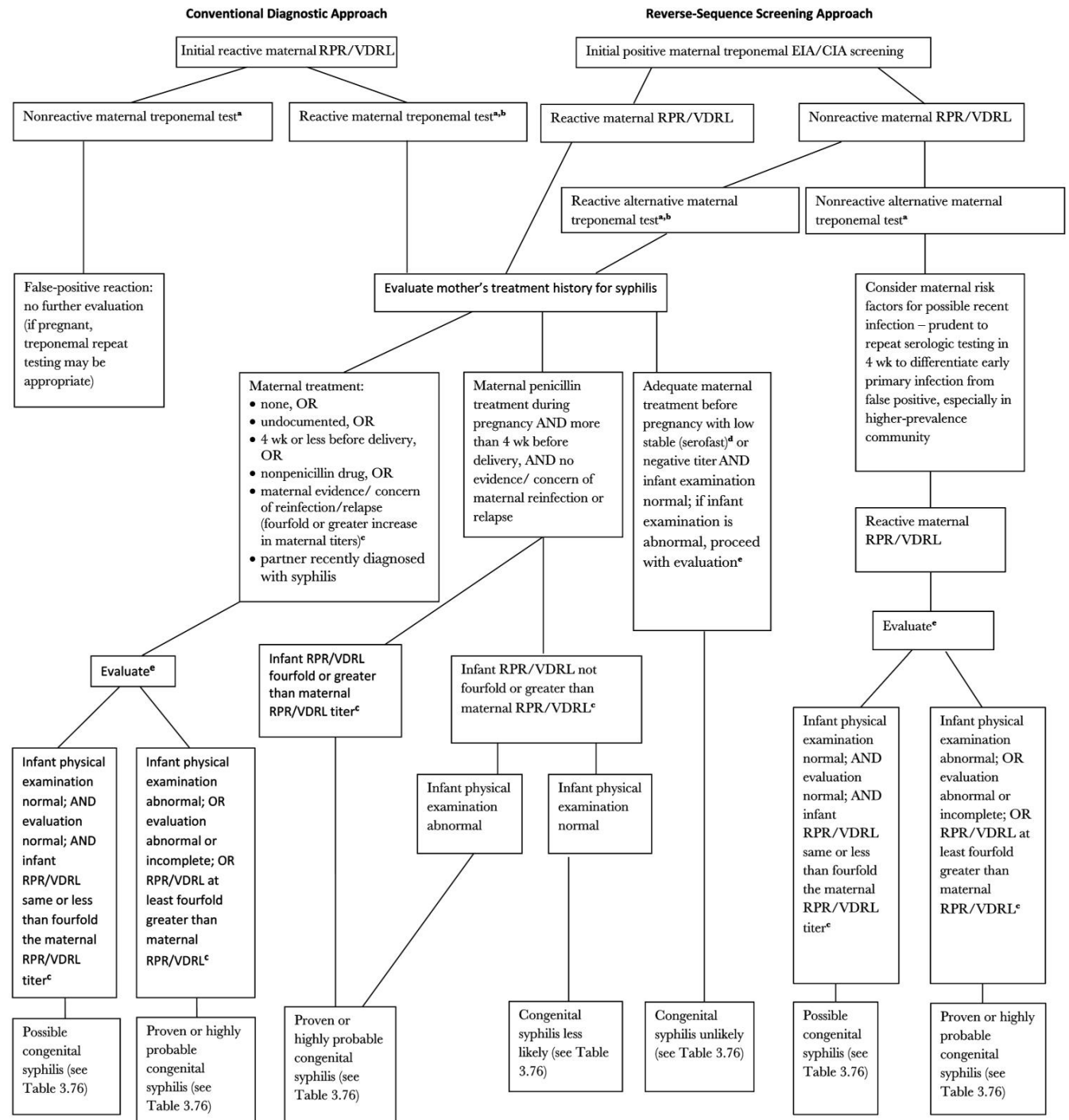
Red Book® 2018, 2018

Figure Legend:

Algorithm for diagnostic approach of infants born to mothers with reactive serologic tests for syphilis.

Date of download:
7/16/2020

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Outcomes of the AAP Algorithm

- **Congenital Syphilis Unlikely**
 - No treatment
- **Congenital Syphilis Less Likely**
 - Single dose of 50,000 units/kg of IM Benzathine Penicillin G
- **Possible Congenital Syphilis**
 - 10 days of IV Penicillin G
- **Highly Probable or Proven Congenital Syphilis**
 - 10 days of IV Penicillin G

Missed Opportunities for Prevention of Congenital Syphilis — United States, 2018

Anne Kimball, MD^{1,2}; Elizabeth Torrone, PhD²; Kathryn Miele, MD^{2,3}; Laura Bachmann, MD²; Phoebe Thorpe, MD²; Hillard Weinstock, MD²; Virginia Bowen, PhD²

TABLE 2. Missed congenital syphilis prevention opportunities among mothers of infants with congenital syphilis, by U.S. Census region* — United States, 2018

Missed prevention opportunity	Census region No. (% [†])				
	Total	South	West	Midwest	Northeast
No timely prenatal care and no timely syphilis testing	368 (28.2)	136 (19.9)	191 (41.1)	25 (24.3)	16 (30.2)
No timely syphilis testing despite receipt of timely prenatal care	116 (8.9)	47 (6.9)	55 (11.8)	8 (7.8)	6 (11.3)
No adequate maternal treatment despite a timely syphilis diagnosis	401 (30.7)	235 (34.3)	133 (28.6)	26 (25.2)	7 (13.2)
Late identification of seroconversion during pregnancy [‡]	146 (11.2)	73 (10.7)	30 (6.5)	22 (21.4)	21 (39.6)
Missed prevention opportunity not identified					
Clinical evidence of congenital syphilis despite maternal treatment completion [¶]	46 (3.5)	33 (4.8)	9 (1.9)	4 (3.9)	0 (0.0)
Insufficient information ^{**}	229 (17.5)	161 (23.5)	47 (10.1)	18 (17.5)	3 (5.7)
Total	1,306	685	465	103	53

* *South*: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia; *West*: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming; *Midwest*: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin; *Northeast*: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont.

[†] Percentages might not sum to 100 because of rounding.

[‡] Must have had a negative syphilis test early in pregnancy and a positive syphilis test <30 days before delivery, at day of delivery, or ≤90 days after delivery to be classified as having a seroconversion during pregnancy.

[¶] Infant indications of infection include direct detection of *Treponema pallidum* by dark field microscopy or special stains; a reactive nontreponemal test and any one of these signs or symptoms of congenital syphilis: condyloma lata, snuffles, syphilitic rash, hepatosplenomegaly, jaundice/hepatitis, pseudoparalysis, or edema on physical exam; long-bone radiograph findings consistent with congenital syphilis; abnormal protein or white blood cell count in the cerebrospinal fluid; or reactive venereal disease research laboratory test in the cerebrospinal fluid.

^{**} Insufficient information submitted to CDC related to maternal prenatal care, testing, or treatment to categorize.

History Discovered after Diagnosis

- **Mother had a negative first trimester screen for syphilis in the first trimester.**
- **Mother was not rescreened in the second trimester.**
- **Mother had an unusual diffuse rash at 30 weeks gestation consistent with secondary syphilis.**
- **Mother denied new sexual partners during the pregnancy.**
- **Father had been treated for Gonorrhea two years prior. He was not screened for syphilis at that time.**

Primary Syphilis on the Rise

The North Dakota Department of Health (NDDoH) is reporting an increase in the number of primary syphilis cases, which demonstrates that transmission is occurring in the state. There have been seven reported cases of primary syphilis in July - August 2019 which is equal to the total number of reports from January - June 2019. The majority of the recent cases have resided in Cass County and are in both men and women. Primary syphilis is the first stage of the infection and is highly infectious. It typically presents with a painless lesion, also known as a chancre, and occurs at the anatomical site in which the bacterium enters the body. However, in some instances the chancre cannot be seen due to its location. Risk factors for these infections have been noted among men who have sex with men, persons who inject drugs and/or people reporting anonymous sexual partners.

Action Items:

Local and Tribal Health Departments: Please forward this health advisory to all healthcare providers in your jurisdiction.

Hospitals and Clinics: Please forward this health advisory to all infectious disease, primary care, OB/GYN, and emergency/urgent care providers.

Health Care Providers:

- Obtain a complete sexual risk history of all patients.
- Test for syphilis and other STDS, including HIV, for all persons with high-risk sexual behaviors.
- Test and treat patients presumptively with symptoms suggestive of primary or secondary syphilis.
- Test and treat patients presumptively when exposed to syphilis.
- Test all pregnant persons at the first prenatal visit, at 28-32 weeks and then at delivery, regardless of risk.

July 13, 2018

HEALTH ADVISORY

Recommendation for Syphilis Screening Among Pregnant Women

The North Dakota Department of Health (NDDoH) is alerting healthcare providers in North Dakota about the rise of syphilis infections across all areas of the state. There was a 24% increase in cases from 2016 to 2017. As the total case counts have increased, so has the proportion of cases among women, especially those of childbearing age. In 2016 and 2017, women accounted for 15% and 22% of all syphilis cases. So far in 2018, women have accounted for 28% (12 cases) of all reported syphilis cases. The increase of cases among women is of concern due to the possibility of transmission to an unborn child (congenital syphilis), which can result in serious complications or death of the baby. Many of these women did not know they were at risk for syphilis due to unknown risk factors of their partners. Nationwide, congenital syphilis cases have increased 86.9% from 2012 to 2016, with 628 reported cases, including 41 syphilitic stillbirths in 2016.

Currently, all pregnant women are screened for syphilis in the first trimester. The NDDoH, following CDC guidance, is recommending pregnant women also be screened twice during the third trimester, once at 28-32 weeks gestation and again at delivery. Any woman who has a fetal death after 20 weeks gestation should be tested for syphilis. Surrounding states have found success in identifying syphilis infections late in pregnancy with this recommendation.

Action Items:

Local and Tribal Health Departments: Please forward this health advisory to all healthcare providers in your jurisdiction.

Hospitals and Clinics: Please forward this health advisory to all OB/GYN, infectious disease, primary care and emergency/urgent care providers.

Health Care Providers:

- Screen all pregnant women for syphilis in the first trimester, at 28-32 weeks gestation and at delivery.
- Pregnant women should be treated at the time of diagnosis with the penicillin regimen appropriate for the stage of infection (Table 1). Penicillin G is the only known antimicrobial for preventing maternal transmission to the fetus.
- An adequate response to treatment should be monitored throughout pregnancy.
- For pregnant women diagnosed with syphilis, information concerning ongoing risk behaviors and treatment of sex partners should be obtained to assess the risk for reinfection.

Missed Opportunities for Intervention

- **Father's past evaluation for Gonorrhea did not trigger screening for syphilis.**
- **Mother's rash was not recognized as secondary syphilis.**
- **North Dakota recommendations for syphilis screening during pregnancy at 28-32 weeks gestation and at delivery were not followed.**
- **Stigmata were missed after nursery discharge.**

Conclusions

- **Missed congenital syphilis is devastating and should be a never event.**
- **Hospitals in North Dakota need to do better about following screening guidelines for syphilis for both pregnant women and sexually active adults.**
- **If OB/GYN providers do not perform appropriate screening, nursery providers should consider screening neonates for syphilis**
- **Providers caring for neonates should familiarize themselves with stigmata of congenital syphilis.**

Thank You to Our Speaker!

- Dr. Clifford Mauriello

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Next Lunch and Learn: August 26th at 12pm CT

- *HIV and Viral Hepatitis and COVID-19*

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